FORM PTO-1390 (REV. 9-2001) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY 'S DOCKET NUMBER: 43531

U.S. APPLICATION NO. (If known, see 37 CFR 1.5): 10/070656

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/EP 00/08875	08 SEPTEMBER 2000	10 SEPTEMBER 1999

TITLE OF INVENTION
AN ANTI-OXIDANT PREPARATION BASED ON PLANT EXTRACTS FOR THE TREATMENT OF CIRCULATION AND ADIPOSITY PROBLEMS

APPLICANT(S) FOR DO/EO/US
Gianfranco MERIZZI

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☑ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☐ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and (21) indicated below.
4. ☐ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☑ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☑ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International Application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☐ Amendments to the claims of the International Aplication under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☐ are attached hereto (required only if not communicated by the International Bureau).
   b. ☐ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371 (c)(3)).
9. ☐ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English lanugage translation of the annexes of the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11 to 20 below concern document(s) or information included:

11. ☑ An Information Disclosure Statement under 37 CFR 1.97 and 1.98.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☐ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 1.821 - 1.825.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).
20. ☑ Other items or information:

Initial Information Data Entry Sheet

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/070656	PCT/EP00/08875	43531

21. ☑ The following fees are submitted:	CALCULATIONS PTO USE ONLY	
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):		
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$1040.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$890.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$740.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$710.00**		
International preliminary examination fee (37 CFR 1.482) paid to USPTO and all claims satisfied provisions of PCT Article 33(1)-(4) **$100.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	- 20 =	0	x **$18.00**	$
Independent claims	- 3 =	0	x **$84.00**	$
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ **$280.00**	$

TOTAL OF ABOVE CALCULATIONS =	$	
☐ Applicant claims small entity status. See 37 CFR 1.27. The fees indicated above are reduced by 1/2. +	$	
SUBTOTAL =	$ 890.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).	$	
TOTAL NATIONAL FEE =	$ 890.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$	
TOTAL FEES ENCLOSED =	$ 890.00	
	Amount to be refunded:	$
	charged:	$

a. ☑ A check in the amount of $ 890.00 to cover the above fees is enclosed.

b. ☐ Please charge my Deposit Account No. 18-2220 in the amount of $ _____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. ☑ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 18-2220 . A duplicate copy of this sheet is enclosed.

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137 (a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

Roylance, Abrams, Berdo & Goodman LLP

1300 19th Street, N.W., Suite 600

Washington, DC 20036

(202) 659-9076

SIGNATURE

Lance G. Johnson

NAME

32,531 3/8/02

REGISTRATION NUMBER

Applicant or Patentee:
Serial or Patent No.:
Filed or Issued:
For:

Attorney's Docket No.: _____

VERIFIED STATEMENT (DECLARATION) CLAIMING SMALL ENTITY STATUS
(37 CFR 1.9(f) and 1.27(c)) — *SMALL BUSINESS CONCERN*

I hereby declare that I am

[ ] the owner of the small business concern identified below:
[ ] an official of the small business concerned empowered to act on behalf of the concern identified below:

NAME OF CONCERN CETERIS HOLDING B.V. – AMSTERDAM (OLANDA) – SUCCURSALE DI LUGANO
ADDRESS OF CONCERN Via Serafino Balestra 27
CH-6900 LUGANO (Switzerland)

I hereby declare that the above identified small business concern qualifies as a small business concern as defined in 13 CFR 121.3-18, and reproduced in 37 CFR 1.9(d), for purposes of paying reduced fees under section 41(a) and (b) of Title 35, United States Code, in that the number of employees of the concern, including those of its affiliates, does not exceed 500 persons. For purposes of this statement, (1) the number of employees of the business concern is the average over the previous fiscal year of the concern of the persons employed on a full-time, part-time or temporary basis during each of the pay periods of the fiscal year, and (2) concerns are affiliates of each other when either, directly or indirectly, one concern controls or has the power to control the other, or a third party or parties controls or has the power to control both.

I hereby declare that rights under contract or law have been conveyed to and remain with the small business concern identified above with regard to the invention, entitled "An anti-oxidant preparation based on plant extracts for the treatment of circulation and adiposity problems"

by inventor(s)
Gianfranco MERIZZI
described in:

[ ] the specification filed herewith
[X] application serial no. PCT/EP00/08875 , filed September 8, 2000
[ ] patent no. , issued

If the rights held by the above identified small business concern are not exclusive, each individual, concern or organization having rights to the invention is listed below* and no rights to the invention are held by any person, other than the inventor, who could not qualify as a small business concern under 37 CFR 1.9(d) or by any concern which would not qualify as a small business concern under 37 CFR 1.9(d) or a nonprofit organization under 37 CFR 1.9(e). *NOTE: Separate verified statements are required from each named person, concern or organization having rights to the invention averring to their status as small entities. (37 CFR 1.27)

FULL NAME _____
ADDRESS _____

[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NON PROFIT ORGANIZATION

FULL NAME _____
ADDRESS _____

[ ] INDIVIDUAL [ ] SMALL BUSINESS CONCERN [ ] NON PROFIT ORGANIZATION

I acknowledge the duty to file, in this application or patent, notification of any change in status resulting in loss of entitlement to small entity status prior to paying, or at the time of paying, the earliest of the issue fee or any maintenance fee due after the date on which status as a small entity is no longer appropriate. (37 CFR 1.28(b))

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application, any patent issuing thereon, or any patent to which this verified statement is directed.

NAME OF PERSON SIGNING LUIGI ZANETTI
TITLE OF PERSON OTHER THAN OWNER DIRECTOR
ADDRESS OF PERSON SIGNING VIA MONTALBANO 9, 6900 LUGANO(SWITZERLAND)

SIGNATURE _____ DATE April 30, 2002

An anti-oxidant preparation based on plant extracts for the treatment of circulation and adiposity problems

The present invention relates to a preparation based on plant extracts which has an anti-oxidant effect and is particularly useful in the treatment of circulation problems such as phlebitis, varicose veins, arteriosclerosis, haemorrhoids and high blood pressure, as well as in the prevention and treatment of surplus fat.

The object of the invention is to provide a preparation to be taken orally, based on a combination of active ingredients of natural and plant origin, which work more effectively to prevent and treat the aforesaid problems when administered by mouth.

This object is achieved according to the invention by providing a preparation characterised in that its active ingredients include a combination of *Ginkgo biloba* biflavones, catechine and/or epicatechine, cumarine and derivatives thereof, iodine and an ingredient chosen from asiaticoside, asiatic acid, madecassic acid and compounds thereof.

The preparation is obtained by mixing plant extracts which contain the above active components.

It is known that extracts from the leaves of *Ginkgo biloba* contain important active components and in particular flavonol glucosides, lactonic terpenes and dimeric biflavones or flavones. The flavonol glucosides and the lactonic terpenes constitute the active components of the standardized *Ginkgo biloba* extracts currently available on the market;

however these extracts do not contain the biflavone component which is not extracted during normal processing. The *Ginkgo biloba* extract used in compositions according to the present invention is highly enriched with the biflavone component and, as a possible option, with extracts containing flavonol glucosides and lactonic terpenes. Five biflavones in particular have been identified in the biflavone component of *Ginkgo biloba*: these are, in particular, amentoflavone, bilobetine, isoginkgetine, ginkgetine and sciadopisitine; the five said compounds differ only by the presence of methyl groups in some positions and, like all flavones, are powerful antioxidants. However, from a pharmacological point of view, they are characterised by their anti-phosphodiesterase, anti-inflammatory, vasculokinetic and anti-allergy properties. Phosphodiesterases (PDE) are cellular enzymes responsible for interacting with cyclic nucleotides so as to linearize them. Cyclic nucleotides are involved as second messengers in transmitting intercellular signals and are thus responsible for some phenomena which are very important from a biochemical point of view. They assist with the visual process and in the relaxation of smooth muscles, they stimulate lipolysis in adiposity and vasculo-motion in capillary arterioles. More specifically, it is sufficient to report that in inhibiting PDE depending on cyclic AMP, these biflavones demonstrate an IC50 of 1.2 micromoles.

The anti-inflammatory properties of biflavones, and in particular those of amentoflavone, have been demonstrated both in vitro, by measuring the interaction of these biflavones with cyclo-oxygenase, lipo-oxygenase and phospho-lipase A2, and in vivo, using various models of inflammation in animals (carragineen oedema, Croton oil inflammation etc). The anti-inflammatory action of the biflavones was confirmed

both in models using local application and in those in which they were administered peritoneally. In these models, the biflavones always demonstrated an anti-inflammatory action equivalent to that of indomethacyn or prednisolone. This effectiveness can be explained by analysing the IC50 of cycol-oxygenase inhibition, which for amentoflavone is 3 micromoles.

With regard to the microvasculokinetic activity of biflavones, it should be reported that, following acute treatment, these substances improve the size of the arterial sphygmic wave and, following chronic treatment they improve capillary density in tissues with trophic-connective problems, such as those affected by panniculopathy and/or various degrees of sclerodermy. Biflavones also have clear anti-allergy properties; they inhibit the release of histamine by mast-cells stimulated by allergens.

In the context of the present invention, it has been demonstrated that, when administered orally, the activity of the aforesaid biflavones, possibly in combination with flavonol glucosides and lactonic terpenes which are normally present in standard *Ginkgo biloba* extracts, is enhanced when the latter are combined with the aforesaid active compounds.

The extracts are preferably used in a phytosomal form, in which the active components are compounded with phospholipids.

In the context of the invention it is convenient to use an extract of leucocyanidine or leucoanthocyanine derived from *Vitis vinifera* as the source of catechine or epicatechine. Leucoanthocyanines are procyanidolic oligomers derived from

condensing monomeric units of flavan-3-ols and flavan-3,4-diols, these being either free or esterified with gallic acid. Leucocyanines are powerful anti-oxidant substances with the ability to protect capillaries by increasing oxygen to the tissue; these active substances prove biologically active even when administered orally and they have been shown to be tropic for the cardio-vascular system and for all tissues, such as artery walls, which are rich in glucoaminoglycene. Preferably, phytosomal forms of extracts are used, thus further enhancing the bioavailability of the active principles. In this form the procyanodines are completed with phospholipids, particularly distearylphosphatidycoline of soya.

The preferable source of cumarine is an extract of Melilotus (Melilotus officinalis), cumarine and its derivatives being the main active ingredients thereof; the main active ingredients of this extract are melilotine (3,4 dihydro-cumarine), melilotic acid (hydroxycumarinic acid), melilotoxide (a melilotine glucoside) and some flavinoids which act like vitamin P; the active ingredients contained in the extract are particularly effective in increasing capillary strength, in reducing vascular permeability, in stimulating venous circulation and improving lymphatic circulation.

Extract of Melilotus may be replaced or backed up, as a source of cumarine and its derivatives, by an extract of *Aesculus hippocastanum* (horse chestnut) in the same dosage or up to around twice the dose of Melilotus extract.

The most abundant active principle of *Aesculus hippocastanum* extract, obtained from the bark, the pericarp of the fruit,

the leaves or the buds, is cumarine glucoside, esculoside (6-0-glucosil-7-hydroxy-cumarine). Other cumarines contained in the extract are fraxine (8-0-glycoside-7-hydroxy-6-metoxycumarine) and the aglicones, esculetin (6,7-dioxy-cumarine) and fraxetine (7,8-dioxy-6-methoxy-cumarine).

The preferred source of asiaticoside, asiatic acid and madecassic acid is an extract containing a triterpenic fraction of centella (*Centella Asiatica*) which contains a combination of the above three active principles. The extract should preferably be used in a phytosomal form, obtained by a reaction between the triterpenic fraction of *Centella Asiatica* with a phospholipid. A main action of the triterpenic fraction of centella consists in accelerating the uptake and metabolism of lysine and of proline, thus increasing the synthesis and the release of tropocollagen and stimulating the turnover of acid mucopolysaccharide acids in connective tissue. Thanks to these properties, the active principles are particularly effective in reducing localised adiposity.

The preferred source of iodine is an extract of *Fucus vesiculosus*, a seaweed of the Fucaceae family. The role of the iodine in *Fucus vesiculosus* is currently well characterised; it is made more readily available by complexing with a protein fraction of the extract; it increases the synthesis of thyroid hormones and indirectly enhances the lipolitic action of these hormones (T3 and T4) thanks to a local thermogenic action on adipose tissue. The Fucus extract also contains polysaccharides such as fucoidin, alginic acid, laminarin and poliose; of these, the alginic acids, in particular, enhance the effect of the extract since they are hydrophilic molecules able to swell from their

original volume in the presence of water; thanks to this characteristic, when ingested they not only reduce the appetite but also increase the speed of transit of food through the intestines, thus ensuring that it is less well absorbed.

The basic composition of the invention can thus be obtained by mixing a biflavone extract of *Ginkgo biloba* (perhaps in combination with a standard *Ginkgo biloba* extract also containing flavonol glucosides and lactonic terpenes), leucocyanidine extract, Melilotus extract, Centella extract and extract of *Fucus vesuculosus*; these extracts preferably being in a phytosome form.

With reference to the extracts normally available on the market, the basic composition is preferably made up by the following percentages by weight:

1.5 - 32% biflavone extract of *Ginkgo biloba*;

6 - 80% of leucocyanidine extract;

1.5 - 60%, preferably 1.5 - 32% of melilotus extract and/or *Aesculus hippocastanum* extract;

1.5 - 32% of centella extract;

1.5 - 85% *Fucus vesiculosus* extract, possibly in combination with:

1.5 - 32% of standard *Ginkgo biloba* extract containing flavon glucosides and lactonic terpenes.

In terms of the content of active principles, the composition of the invention preferably contains the following percentages by weight:

0.2 - 12%, preferably 0.5 - 6% of total biflavones, expressed as ginkgetine content;

0.2 - 12%, preferably 0.5 - 8% of catechine and/or epicatechine, expressed as catechine content;

0.15 - 7%, preferably 0.3 - 3.5% of cumarine and its derivatives;

0.25 - 15%, preferably 0.5 - 7.5% of asiaticoside;

0.25 - 22%, preferably 0.5 - 11 % of asiatic acid and/or madecassic acid;

up to 0.5% of iodine and possibly one or more of its components:

0.25 - 12%, preferably 0.5 - 6%, of flavonol glucosides, and

0.1 - 2%, preferably 0.2 - 1% of Ginkolide lactonic terpenes (bilobalide).

The composition can also contain active ingredients chosen from methylxanthinic derivatives, such as caffeine, theobromine or theophylline in particular; mono and di-caffeoylchinic acids, chlorogenic acids, eicosapentaenoic acid (EPA), docahexaenoic acid (DHA) gamma-linolenic acid and combinations thereof.

The preferred source of methylxanthinic derivatives, of caffeine and of chlorogenic acids in particular, is an extract of *Ilex paraguariensis*, possibly in phytosomal form; the standard, commercially available extract can be added to the previously-described basic mixture in a quantity of 1.5 to 32% by weight.

Caffeoylchinic acid and its derivatives (such as cynarine) are preferably introduced by means of an artichoke extract (*Cynara scolymus*); this extract typically also contains caffeic acid and chlorogenic acid; this extract is preferably

used in quantities of 1.5 to 32% by weight with reference to 100 parts of the basic mixture.

The preferable source of eicosapentaenoic acid (EPA) and of docohexaenoic acid (DHA) is fish oil which, with reference to 100 parts of the basic mixture, may be added in quantities of 5 to 80% by weight.

Gamma-linolenic acid is preferably introduced into the formulation by the use of borage oil, added in quantities of 30 to 120% by weight with reference to 100 parts of basic preparation.

In particular, in the preferred embodiment of the invention, the composition includes one or more of the following components:

Caffeine in quantities of 0.05 to 2.5 (preferably 0.1 - 1%) by weight with reference to the total preparation,

Caffeoylchinic acids in quantities from 0.05 to 4.8% (preferably 0.01 to 2.5%) by weight,

Eicosapentanoic acid in quantities from 0.75 to 24% (preferably from 1.5 to 12%) by weight,

Docohexanoic acid in quantities from 0.6 to 8% (preferably 1.2 to 4%) by weight,

Gamma-linolenic acid in quantities from 2.5 to 22%, preferably 5-11% by weight.

For example, a typical composition could be formulated according to the data in the table below, which gives the preferred minimum and maximum quantities expressed in parts by weight of the components of the basic mixture (marked with an asterisk) and of optional ingredients.

	Minimum (Parts by weight)	**Maximum** (Parts by weight)
*Dry extract of *Vitis vinifera* (optionally phytosomes)	20	200
*Dry extract of Melilotus officinalis and/or Aesculus hippocastanum	5	40
**Ginkgo biloba* biflavones (optionally phytosomes)	5	50
Dry extract of *Ginkgo biloba* (optionally phytosomes)	5	50
*Dry extract of *Fucus vesiculosus*	50	200
*Dry extract of *Centella asiatica* (optionally phytosomes)	10	50
Dry extract of artichoke	10	100
Dry extract of *Ilex paraguariensis*	10	100
Borage oil	50	1000
Fish oil	50	750
Soya lecithin	20	100

In the above table, the given values, expressed in parts by weight, correspond, when expressed in milligrams to the minimum and maximum daily doses recommended or to the dose per capsule.

The composition of the invention is formulated in forms suited to be taken orally, such as, for example, gelatin capsules with either soft or rigid shells, tablets, pills, elixirs, suspensions and syrups. The various forms can include excipients and/or binders and/or pharmaceutically acceptable vehicles, in particular lecithin mono- and di-glycerides of fatty acids. The mixture of extracts can be administered orally, possibly in an edible vehicle or can be incorporated directly into food as part of a diet.

The preparation is particularly useful in treating localised adiposity, in particular in men but also in women. It is well known that adiposity differs in men and in women, by the area in which it is deposited, by the quantity, by functional response and by consequences for health; in actual fact this surplus fat ("spare tyres" in men and cellulite in women) is due, at least in part, to a tropism which is known to involve both vascular and connective tissue, as well as adispose tissue. The composition of the invention provides an association of well characterised substances from a pharmaco-toxicological and chemical point of view, which is totally free of side effects and is particularly advantageous compared to pharmaceutical preparations based on appetite-suppressant compounds, as used in conventional pharmacological treatment.

CLAIMS

1. A composition based on plant extracts, with an anti-oxidant activity which is particularly useful in the prevention and treatment of circulation problems and in the prevention and treatment of adiposity, characterised in that its active ingredients comprise, in association, biflavones of *Ginkgo biloba*, catechine and/or epicatechine, cumarine or derivatives thereof, iodine and a component chosen from among madecassic acid, asiatic acid, asiaticoside and mixtures of these.

2. A composition according to Claim 1, characterised in that it is obtained by mixing plant extracts containing the aforesaid active principles.

3. A composition according to Claim 2, charcaterised in that the said extracts are in phytosomal form.

4. A composition according to any one of the preceding Claims, characterised in that it further includes flavonol glucosides and lactonic terpenes.

5. A composition according to any Claim from 1 to 4, characterised in that it also includes an active principle chosen from the group consisting of methylxanthinic derivatives, chlorogenic acids, mono- and di-caffeoylchinic acid and derivatives thereof, eicosapentaenoic acid, docohexaenoic acid, gamma-linolenic acid and mixtures thereof.

6. A composition according to any of Claims 1 to 4, characterised in that it is obtained by mixing plant extracts in the following percentages by weight:

1.5-32% of *Ginkgo biloba* biflavone extract;

6-80% of leucocyanidine;

1.5-32% of *Melilotus* and/or *Aesculus hyppocastanum* extract;

1.5-32% of centella extract;

1.5-85% extract of *Fucus vesiculosus*; and optionally

1.5-32% of standardised *Ginkgo biloba* extract containing flavone glucosides and lactonic terpenes.

7. A composition according to Claim 6, characterised in that with reference to 100 parts of the basic mixture of Claim 6, it also includes one or more of the following components:

from 1.5 to 32% by weight of *Ilex paraguariensis* extract;

from 1.5 to 32% by weight of artichoke extract;

from 5 to 80% by weight of fish oil;

and

from 30 to 120% by weight of borage oil.

8. A composition according to any one of the preceding Claims which includes:

0.12-12%, preferably 0.5-6% by weight, of total biflavones;

0.2-12%, preferably 0.5-8% by weight, of catechine and/or epicatechine;

0.15-7%, preferably 0.3-3.5% by weight, of cumarine and derivatives thereof;

0.25-15%, preferably 0.5-7.5% by weight of asiaticoside;

0.25-22%, preferably 0.5-11% by weight, of asiatic acid and/or madecassic acid;

up to 0.5% of iodine and, optionally

0.25-12%, preferably 0.5-6% by weight, of flavonol glucosides and

0.1-2%, preferably 0,2-1% by weight, of lactonic terpenes.

9. A composition according to Claim 8, characterised in that it also includes one or more of the following components:

from 0.05 to 2.5%, preferably 0.1-1% by weight, of caffeine;

from 0.05 to 4.8%, preferably 0.1-2.5% by weight, of caffeilchinic acids;

from 0.75 to 24%, preferably 1.5-12% by weight, of eicosapentaenoic acid;

from 0.6 to 8%, preferably 1.2-4% by weight, of docoesaenoic acid; and

from 2.5 to 22%, preferably from 5 to 11% by weight of gamma-linolenic acid.

10. A composition according to any one of the preceding Claims in a pharmaceutical form for oral administration.

11. The use of flavone dimers in the formulation of a preparation based on plant extracts useful in the prevention and treatment of circulation problems and adiposity.

ABSTRACT

An anti-oxidant preparation based on plant extracts useful for circulation problems and surplus fat deposits

A preparation based on plant extracts, with an anti-oxidant action which is particularly useful in the prevention and treatment of circulation problems and in the prevention and treatment of surplus fat deposits, characterised in that its active ingredients comprise, in association, *Ginkgo biloba* biflavones, catechine and/or epicatechine, iodine and a component selected from among madecassic acid, asiatic acid, asiaticoside or combinations thereof.

43531

DECLARATION AND POWER OF ATTORNEY

As below-named inventors, I hereby declare that our residences, post office addresses and citizenship are as stated below next to our names; I believe I am the original, first and joint inventors of the subject matter which is claimed and for which a patent is sought on the invention entitled AN ANTIOXIDANT PREPARATION BASED ON PLANT EXTRACTS FOR THE TREATMENT OF CIRCULATION AND ADIPOSITY PROBLEMS described in the specification filed herewith.

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendments(s) referred to above.

I acknowledge the duty to disclose information which is material to the examination of this application in accordance with Title 37, Code of Federal Regulations, §1.56(a).

I hereby claim foreign priority benefits under Title 35, United States Code §119 of any foreign application(s) for patent or inventor's certificate or of any PCT international application(s) designating at least one country other than the United States of American listed below and have also identified below any foreign application(s) for patent or inventor's certificate or any PCT international application(s) designating at least one country other than the United States of America filed by us on the same subject matter having a filing date before that of the application(s) on which priority is claimed:

Prior Foreign Application(s)			Priority Claimed
Application No.	Country	Date Filed	Yes No
PCT/EP 00/08875	WO	08 September 2000	X
1663/99	CH	10 September 1999	X

I hereby declare that all statements made herein of our own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I hereby appoint David S. Abrams, Reg. No. 22,576; Robert H. Berdo, Reg. No. 19,415; Alfred N. Goodman, Reg. No. 26,458; Mark S. Bicks, Reg. No. 28,770; John E. Holmes, Reg. No. 29,392; Lance G. Johnson, Reg. No. 32,531; Dean H. Nakamura, Reg. No. 33,981; Garrett V. Davis, Reg. No. 32,023; Stacey J. Longanecker, Reg. No. 33,952; Joseph J. Buczynski, Reg. No. 35,084; Tara Laster Hoffman, Reg. No. 46,510; Jeffrey J. Howell, Reg. No. 46, 402; Aisha Ahmad, Reg. No. 47,381; Marcus R. Mickney, Reg. No. 44,941; Christian C. Michel, Reg. No. 46,300; Mark W. Hrozenchik, Reg. No. 45,316; Peter L. Kendall, Reg. No. 46,246; Daryl A. Basham, Reg. No. 45,869; and Julie R. Keller, Reg. No. 30,488, all of Roylance, Abrams, Berdo & Goodman, L.L.P., whose address is 1300 19th Street, N.W., Suite 600, Washington, DC 20036, telephone number (202) 659-9076, our attorneys and/or agents with full power of substitution and revocation, to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith.

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